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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/509,612	03/29/2000	SERGIO ABRIGNANI	0366.103	7749

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EXAMINER
WORTMAN, DONNA C

ART UNIT	PAPER NUMBER
1648	22

DATE MAILED: 05/09/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

S.M.

Office Action Summary	Application No.	Applicant(s)	
	09/509,612	ABRIGNANI ET AL.	
	Examiner	Art Unit	
	Donna C. Wortman, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 March 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7,29,31 and 32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7,29,31 and 32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Claim 7 was amended in Paper No. 24. Claims 7, 29, 31 and 32 are pending and under examination.

The claims are drawn to a method for inhibiting binding of the E2 protein of HCV to human cells comprising administering to a human infected with HCV an amount of a CD81 protein effective to bind HCV, where the CD81 protein comprises amino acids 113-201 of the human CD81 amino acid sequence depicted in SEQ ID NO:21, to inhibit binding of HCV to human cells.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 7, 29, 31 and 32 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention, essentially for reasons already of record.

Applicant has made reference to the test for enablement as set out in In re Wands, 858 F.2d 731, 737, 8 USPQ2d, 1400, 1404 (Fed. Cir. 1988), and has argued (1) that it is not necessary to demonstrate that the invention is beneficial to a human to fulfill the enablement requirement. Applicant has asserted (2) that the claims and written description comply with the utility requirement in that Applicant has demonstrated that CD81 binds the E2 portion of HCV, and that there is a reasonable correlation between the binding of CD81 to HCV, and the asserted utility, inhibiting binding of HCV to human cells. Applicant has argued

(3) that no factual evidence need be presented that administration of a CD81 to a human infected with HCV would inhibit binding of HCV to human cells; (4) that case law and the MPEP do not require a factual basis for concluding that *in vitro* results can be extrapolated to an *in vivo* benefit; (5) that MPEP 2164.03 provides that results from an *in vitro* model in the specification constitute a working example if that example "correlates" with the claimed method; (6) that Example 7 in the specification is a working example; (7) that since the only animal model of HCV infection is a chimpanzee model and HCV does not readily propagate in tissue culture, a person of skill in the art would accept that the *in vitro* data presented could be used to predict a beneficial effect in a human, i.e., a person of skill in the art would accept that *in vitro* data reasonably correlate to a beneficial effect in a human infected with HCV; and (8) that Applicants believe that it is not necessary to provide a factual basis for correlating *in vitro* results with an *in vivo* benefit.

Applicant's arguments have been considered but not found persuasive. With respect to point (1), Applicant's remarks are not understood, since the claims are clearly drawn to a pharmaceutical use of a CD81 protein, i.e., a treatment method, as claim 7 recites that the protein is administered to a human infected with HCV and inhibits binding of HCV to human cells. The claimed use must be enabled in accordance with 35 USC 112, first paragraph. With respect to point (2), it is noted that no rejection was made under 35 USC 101, for lack of utility; the only outstanding rejection is that under 35 USC 112, first paragraph, as failing to teach how to use. Where Applicant has claimed a process of treating a

certain disease condition with a certain compound and provided a credible basis for asserting that the compound is useful in that regard, but to actually practice the invention as claimed a person skilled in the relevant art would have to engage in an undue amount of experimentation, the claim may be defective under 35 U.S.C. 112, but not 35 U.S.C. 101 (MPEP 2164.07). Considering points (4)-(8), and whether the amount of experimentation required would be undue, as Applicant has pointed out, the Wands factors, especially the nature of the invention, the state of the prior art, the level of predictability in the art, and the existence of working examples are relevant. As to points (3), (4), and (8), in order to overcome a lack of enablement rejection, Applicant must demonstrate by convincing argument and/or evidence that the disclosure, as filed, would have enabled the claimed invention for one skilled in the art at the time of filing; Applicant has not provided a convincing argument for the reasons given here and has offered no evidence that administration of a CD81 to a human infected with HCV would have a beneficial effect. Addressing points (5) and (6), Applicant has provided no basis for concluding that the *in vitro* example provided correlates with the treatment method claimed. With respect to point (7), as Applicant has aptly pointed out, the only animal model of HCV infection is a chimpanzee model and HCV does not readily propagate in tissue culture; these facts are illustrative of the state of the art and tend to support a lack of predictability. Contrary to Applicant's conclusion, the state of the art and the lack of predictability would lead a person of skill in the art to be unlikely to accept that the *in vitro* data presented could be used to predict a beneficial effect in a human and that the *in*

vitro data presented reasonably correlate to a beneficial effect in a human infected with HCV. Claims to treating a human infected with HCV with a CD81 protein represents an embodiment of the invention based on predicted results rather than work actually conducted or results actually achieved. Lack of a working example is a factor to be considered, especially in a case involving an unpredictable and undeveloped art. Since no basis has been established for correlation, the examples provided are not seen to constitute "working examples." The "predictability or lack thereof" in the art refers to the ability of one skilled in the art to extrapolate the disclosed or known results to the claimed invention. If one skilled in the art can readily anticipate the effect of a change within the subject matter to which the claimed invention pertains, then there is predictability in the art. On the other hand, if one skilled in the art cannot readily anticipate the effect of a change within the subject matter to which that claimed invention pertains, then there is lack of predictability in the art. Accordingly, what is known in the art provides evidence as to the question of predictability.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be

calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Donna C. Wortman, Ph.D. whose telephone number is 703-308-1032. The examiner can normally be reached on Monday-Thursday, 7:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Donna C. Wortman, Ph.D.
Primary Examiner
Art Unit 1648

dcw
May 7, 2003